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รายงานผู้ป่วย

A Case Report

Reduction of Perinatal HIV-1 Transmission with Short Course Zidovudine Prophylaxis in Nakornpathom Hospital, Thailand.

การลดอัตราถ่ายทอดเชื้อ เอชไอวี-I จากมารดาสู่ทารก โดยการใช้ Zidovudine ระยะสั้นในโรงพยาบาลนครปฐม

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กลุ่มงานกุมารเวชกรรม โรงพยาบาลนครปฐม

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ABSTRACT

A prospective open labelled study was desinged to evaluate the efficacy of short course prophylactic zidovudine (ZDV) use in late prenatal-perinatal-7 days postnatal regimen and perinatal-6 weeks neonatal regimen. One hundred fifteen asymptomatic HIV-I infected pregnant women were enrolled. Breast feeding was not allowed. The perinatal HIV-I transmission rate was reduced from 20.63% ($\frac{13}{63}$) before ZDV use to 7.69% ($\frac{6}{78}$) in late prenatal perinatal - 7 days postnatal regimen significantly ($p < 0.05$) and reduced to 13.5% ($\frac{5}{37}$) in perinatal 6 weeks neonatal ZDV regimen not significantly ($p > 0.05$). Gender, preterm, mode of delivery and birth weight did not influence the perinatal transmission.

บทคัดย่อ

การศึกษาประสิทธิผลของการใช้ยา Zidovudine (ZDV) ระยะสั้น เพื่อป้องกันการติดเชื้อ เอชไอวี-I จากมารดาสู่ทารก มีมารดาที่ติดเชื้อ เอชไอวี-I เข้าร่วมโครงการ 115 คน 78 คนได้รับ ZDV ตั้งแต่อายุครรภ์ 34-36 สัปดาห์ จนกระทั่งคลอด และบุตรได้รับ ZDV น้ำเชื่อมต่อ 7 วัน ส่วน 37 คน ได้รับ ZDV ขณะคลอด และบุตรได้รับ ZDV น้ำเชื่อม จนครบ 6 สัปดาห์ งดนมมารดา พบว่า ZDV สามารถลดอัตราการติดเชื้อ เอชไอวี-I จากมารดาสู่ทารก จากเดิม 20.63% ($\frac{13}{63}$) ก่อนการใช้ ZDV เป็น 7.69% ($\frac{6}{78}$) ในทารกกลุ่มที่มารดาได้ ZDV ตั้งแต่ก่อนคลอดอย่างมีนัยสำคัญทางสถิติ และ 13.51% ($\frac{5}{37}$) ในทารกที่กลุ่มมารดาได้ ZDV ขณะคลอดและทารกได้รับยาหลังคลอด 6 สัปดาห์ แต่ลดลงไม่มีนัยสำคัญทางสถิติ และพบว่า เพศ การคลอดก่อนกำหนด วิธีการคลอด และน้ำหนักตัว ไม่มีผลต่อการติดเชื้อ

Introduction

The substantial reduction of perinatal HIV transmission demonstrated in the ACTG 076 trial in 1994[1] and modified ACTG 076 regimen[2-4] as well as many modified shorter courses of prophylactic zidovudine (ZDV).[5-10] Short antiretroviral regimens that are given in the peripartum period have been shown to be effective, consistent with the perception that most transmission is acquired near to or during delivery. Data from the Perinatal HIV Prevention Trial in Thailand showed that a longer three-part ZDV regimen is more effective than a shorter three-part ZDV regimen.[9] The addition of 3 days of postnatal infant ZDV to a short antepartum-intrapartum ZDV regimen provides no apparent benefit in non-breastfeeding populations (Perinatal HIV Prevention Trial[9] vs Bangkok Trial[5]). The neonatal post-exposure prophylaxis in the absence of maternal treatment has not been studied in clinical trial, observational datas suggest that 6 weeks of ZDV prophylaxis significantly reduced perinatal HIV transmission rate if it is started within 12 hours of birth.[11,12] In rural part of Thailand many pregnant women have either late prenatal care or no prenatal care so short-course ZDV prophylaxis should be appropriate because of simplicity, feasibility, safety, lower cost and patient compliance while retaining substantial efficacy. Very few studies were reported from Regional Hospital in Thailand. So this prospective open-labelled study was designed in Nakorn pathom Hospital to evaluate the efficacy of short-course prophylactic ZDV use in prenatal-perinatal-postnatal-7 days regimen and perinatal-6 weeks neonatal ZDV regimen.

Material and Method

Between June 1997 and March 2001 all known HIV-I positive pregnant women attending the antenatal clinic and labour room at Nakornpathom Hospital, Thailand were enrolled in the study. They received HIV counseling and counseling about the interaction of HIV infection and pregnancy, the risks and benefits of ZDV prophylaxis then informed consent was obtained.

The inclusion criterias were asymptomatic HIV-I infection pregnant women, gestational age about 34-36 weeks in first group and in second group were no prenatal care HIV-I infection pregnant women.

First group received ZDV 300 mg orally twice a day and every 3 hours in labour until delivery. ZDV syrup 2 mg/kg orally every 6 hours was given to the infants for 7 days.

Second group received ZDV (as soon as HIV- testing reported) 300 mg orally every 3 hours until delivery but some cases did not receive ZDV because HIV-testing results were reported after delivery. Infants received same dose of ZDV syrup as first group for 6 weeks. The drug was begun immediately after the infants had been stabilized. Breast feeding was not allowed and infant formula was provided.

Mothers and infants were assesed for possible drug toxic effects and adverse events according to the ACTG adverse events monitoring guide. The infants were examined at birth, 2 week, 1, 2, 4, 6, 9, 12-18 month of age by pediatricians. They received appropriate vaccination and medical care until the age of 18 months. Co-trimoxazole syrup for

Pneumocystis carinii pneumonia prophylaxis was given at 1 month of age until negative HIV-PCR in two separated specimens or until 1 year of age for HIV infected infants. The peripheral blood specimens were tested for CBC and HIV-PCR (HIV-I proviral DNA and RT-PCR) at 1-2 months and 4 months after birth. HIV-Ab Enzyme immunoassay and CBC were obtained at 18 month of age. The infants were concluded to be HIV infected by at least two positive HIV-PCR specimens or positive HIV-Ab.

Statistical analysis

The results were reported ether as percentages or as means ± SD. Group comparisons were performed with Independent-Samples T - Test. A p-value of less than 0.05 indicated statistical significance.

Results

One hundred fifteen HIV-I infected mothers and infants were enrolled. The first group had 78 pairs of mother-infant and the second group had 37 pairs of mother-infant. In the first group all of the HIV-I infected mothers were asymptomatic and the majority of them graduated at elementary level, lived in pair and had family income < 10,000 baht/ month. Forty nine percents were primiparity and thirty-seven percents were second parity. The majority (96.2%) had full compliance only 3.8% had partial compliance (lost about 1-2 doses). Mean ± S.D. of duration of ZDV prophylaxis in mothers was 26.91 ± 10.15 days. Mean ± S.D. of maternal age was 25.97 ± 5.08 years 76.9% of mothers had vaginal deliveries and 19.6% of mothers had cesarean section deliveries. Maternal characteristics were shown in Table 1. All infants were live born without congenital anomalies. Femal infants were 52.6%, male infants were 46.2%, term infants were 92.3% and preterms were 7.7%. Mean ± S.D. of birth weight was 2,948.88 ± 425.92 gm. They had full compliance about 98.7%. Infected infants were 6 persons from 78 persons (7.69%). Infant characteristics in group 1 were shown in Table 2.

In Table 3, the comparison of characteristics of mothers-infants between uninfected HIV-I infants group and infected HIV-I infants group were the same in maternal age, duration of ZDV in mothers, birth weight, male : female, preterm : term, mode of delivery, and compliance in mothers and infants ($p > 0.05$). In Table 4, perinatal HIV-I transmission rate was shown. Perinatal HIV-I transmission rate of infants were born in June, 1994-June, 1997 (before ZDV prophylaxis was used) was 20.63%. After ZDV prophylaxis was used, perinatal HIV-I transmission rate in June,1997-March,2001 was 7.69% in first group and 13.51% in group 2. It was decreased significantly in the first group ($p < 0.05$) and not significantly in group 2 ($p > 0.05$). No severe adverse effect of ZDV in mothers and infants was detectable. Few mothers and infants were mild anemia. Nausea-vomiting symptoms were detected in few mothers.

Discussion

The results of this study suggest that ZDV prophylaxis in late pregnancy-perinatal-postnatal-7 days regimen is effective to reduce perinatal HIV-I transmission rate as other studies.[5-10] The same regimen in other studies, perinatal HIV-I transmis-

Table 1. Maternal Characteristics in group 1

	Mean ± S.D.	95% Confidence interval
Age (years)	26.0 ± 5	25.0 - 27.0
Gestational age (weeks) started ZDV	35.0 ± 1.2	34.7 - 35.3
Duration of ZDV (days) in mother	26.9 ± 10.1	24.6 - 29.3
No. of Parity	**No.**	**%**
1	38	48.7
2	27	34.6
3	11	14.1
4	1	1.3
5	1	1.3
Compliance		
Full	75	96.2
Partial	3	3.8
Mode of delivery		
Vaginal delivery	60	76.9
Caesarean section	15	19.2
Forcep extraction	1	1.3
Vacuum extraction	1	1.3
Breech assisting	1	1.3
Total	78	100

Table 2. Infant Characteristics in group 1

Birth weight (gm)	**Mean ± S.D.** **2,948.88 ± 425.92** **No.**	**95% Confidence interval** **2,851.56 - 3,046.21** **%**
Live born		
Yes	78	100
No	0	0
Sex		
Male	36	46.1
Female	42	53.9
Gestational age (wk)		
< 37	6	7.7
❑ 37	72	92.3
Birth weight (gm)		
< 2,500	7	9.0
2,500 - 3,500	64	82.0
3,501 - 4,000	7	9.0
Compliance		
Full	77	98.7
Partial	1	1.3
HIV Status		
Uninfected	72	92.3
Infected	6	7.7
Total	78	100

Table 3. Comparison of Characteristics of mothers - uninfected HIV infants and mothers - infected HIV infants in group 1

	Uninfected HIV Infants	Infected HIV Infants	P-value
	n = 72	n = 6	
Maternal age (yrs)	26.20 ± 4.97	23.33 ± 6.06	0.186
Duration of ZDV in mothers (Day)	27.28 ± 10.33	22.67 ± 7.00	0.289
Birth weight (gm)	2,967.21 ± 432.17	2,735.00 ± 289.95	0.202
Male : Female	33 : 39	3 : 3	0.870
Preterm : Term	6 : 66	0 : 6	0.465
Vaginal : Caesarean section delivery	53 : 13	4 : 2	0.851
Full Compliance in mother (%)	96.2	100	0.608
Full Compliance in infants (%)	98.7	100	0.773

Table 4. Perinatal HIV-I Transmission rate

month - yr.	No.	Infected HIV infant	% Transmission rate	P value
June, 1994 - June, 1997	63	13	20.63	
June, 1997 - June, 2001				
*group 1 (late prenatal - perinatal - 7 days neonatal ZDV)	78	6	7.69	0.017
*group 2 (perinatal - 6 weeks neonatal ZDV regimen)	37	5	13.51	0.376

sion rate was 5.75% in Hansudewechakul et al's study,[13] 6.7% in Gulgolgarn et al's study[6] and 7.14% in Luesomboon's study.[7]

In perinatal and 6 weeks-neonatal ZDV prophylaxis regimen, perinatal HIV-I transmission rate (13.51%) was decreased from no ZDV prophylaxis group (20.63%) not significantly ($p > 0.05$). It is similar to Wade et al's[11] study (10% and 9.3%), Thai thummyanon et al's study[14] (10.5%) and Hansudewechakul et al's study (14.7%).[13] Several studies have suggested that elective cesarean section[15-17] reduced perinatal HIV-I transmission rate but cesarean section was not demonstrated in this study because it was not elective cesarean section. Gender, preterm, low birth weight and mode of dilivery were not shown to influence of perinatal HIV-I transmission. Maternal viral load influences to perinatal HIV-I transmission[18,19] but ZDV reduces perinatal HIV-I transmission independent of its effect on the level of the maternal peripheral blood proviral

load[20] so in this study maternal viral load was not determined.

Perinatal and neontal ZDV prophylaxis is one of the choices for HIV-I infected pregnant women who had no prenatal care. Another regimen for this group is a single dose of oral nevirapine administered at the onset of labour to HIV-I infected mothers and to infants within 72 hours of life, significantly lowered the risk of HIV-I perinatal transmission than the effect of a short course of ZDV administered over a similar time period.[21] This regimen should be studied in Thailand to evaluate the efficacy and side effect before implementation in prophylaxis program. Resistance to antiretroviral drugs and combination drugs regimen should be evaluated in next time to avoid failure of prophylaxis.

Conclusion

ZDV prophylaxis in late pregnancy-perinatal-postnatal-7 days regimen is effective and feasible in prevention of perinatal HIV-I transmission. Perinatal and 6 weeks-neonatal ZDV prophylaxis is an alternative prophylaxis in HIV-I infected pregnant women without prenatal care. So all HIV infected pregnant women should be encouraged to have early prenatal care with proper counseling and adequate antiretroviral prophylactic treatment.

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References

1. Conner EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. N Engl J Med 1994 ; 331 : 1173-80.
2. Thisyakorn U, Khongpatthanyothin M, Sirivichayakul S, et al. Thai Red Cross zidovudine donation program to prevent vertical transmission of HIV : the effect of the modified ACTG 076 regimen. AIDS 2000 ; 14 : 2921-7.
3. Chaiyote W. Effectiveness of AZT in prevention of vertical transmission of HIV infection at Prachomklao Hospital, Phetchburi. Reg 4 Med J 2000 ; 185-92.
4. Sheryl LH, Michael KL, Joel EH, W. Scottt Clark, Mare B, Steven RN. Experience with routine voluntary perinatal human immunodeficiency virus testing in an inner city hospital. Pediatr Infect Dis J 2001 ; 20 : 1090-2.
5. Shaffer N, Chuachoowong R, Mock PA, et al. Short-course zidovudine for perinatal HIV-I transmission in Bangkok, Thailand : a randomized controlled trial. Lancet 1999 ; 353 : 773-80.
6. Gulgolgarn V, Ketsararat V, Suwanarat A, et al. Vertical transmission rate and mortality rate in infants born to HIV-infected pregnant women in Lampang Hospital, 1996-1999. Thai J Pediatr 2001 ; 40 : 125-34.
7. Luesomboon W. Successful Prevention of HIV vertical transmission with modification of ACTG 076

protocol in early and late pregnancy at Queen Sawangwattana Memorial Hospital, Chonburi, Thailand. Thai J Pediatr 2001 ; 40 : 179-86.

8. Sakondhavat C, Kiatchooskul P, Kosalaraksa P, et al. Prevention of HIV transmission from mother-to-child in Srinagarind Hospital. J Med Assoc Thai 2001 ; 84 : 1460-6.
9. Lallemant M, Jourdain G, Le Coeur S, et al. Atrial of shortened zidovudine regimens to prevent mother-to-child transmission of human immunodeficiency virus type -1. N Engl J Med 2000 ; 343 : 982-91.
10. Limpongsanurak S, Thaithumyanon P, Chaithongwongwatthana S, et al. Short course zidovudine maternal treatment in HIV-I vertical transmission : Randomized controlled multicenter trial. J Med Assoc Thai 2001 ; 84 (Suppl 1) : S 338-45.
11. Wade NA, Birkhead GS, Warren BL, et al. Abbreviated regimens of zidovudine prophylaxis and perinatal transmission of the human immunodeficiency virus. N Engl J Med 1998 ; 339 : 1409-14.
12. Wade NA, Brikhead GS, Frech PT. Short courses of zidovudine and perinatal transmission of HIV. N Engl J Med 1999 ; 340 : 1042-3.
13. Hansudewechakul R, Achalapong C, Paupanwatana S. Reduction of HIV vertical transmission. Thai J Pediatr 2001 ; 40 : 261-7.
14. Thaithumyanon P, Thisyakorn U, Limpongsanurak S, et al. Intrapartum and neonatal zidovudine treatment in reduction of Perinatal HIV-I transmission in Bangkok. J Med Assoc Thai 2001 ; 84 : 1229-34.
15. The International Perinatal HIV Group. The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1. N Engl J Med 1999 ; 340 : 977-87.
16. The European Mode of Delivery Collaboration. Elective caesarean - section versus vaginal delivery in prevention of vertical HIV-I transmission : a randomized clinical trial. Lancet 1999 ; 353 : 1035-9.
17. Kuntiranont K, Sunthornkachit R, Tunthanatip P, et al. Prevention of vertical HIV transmission : protective effect of elective caesarian section and zidovudine prophylaxis. Com Dis J 2000 ; 26 : 118-25.
18. Dickover RE, Gerratty EM, Herman SA, et al. Identification of levels of maternal HIV-I RNA associated with risk of perinatal transmission : effect of maternal zidovudine on viral load. JAMA 1996 ; 275 : 599-605.
19. The European Collaborative Study. Maternal viral load and vertical transmission of HIV-I : an important factor but not the only one AIDS 1999 ; 13 : 1377-85.
20. Lucia FA, Maureen MG, John WS. Zidovudine administered to women infected with human immunodeficiency virus type 1 and to their neonates reduces pediatric infection independent of an effect on levels of maternal virus J Pediatr 1997 ; 130 : 906-14.
21. Guay LA, Musoke P, Fleming T, et al. Intrapartum and neontal single dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-I in Kampala, Uganda : HIV NET 012 randomised trial. Lancet 1999 ; 354 : 795-802.